Reviewer's report

Title: Persistence of the humoral and cellular immune response of an H5N1 adjuvanted influenza vaccine in elderly persons: two-year follow-up of a randomised open-label study

Version: 2 Date: 2 July 2014

Reviewer: Birgit Weinberger

Reviewer’s report:

The manuscript “Persistence of the humoral and cellular immune response of an H5N1 adjuvanted influenza vaccine in elderly persons: a two-year follow-up study of a randomized open-label study” adds long-term follow-up data to a previously published clinical trial. The induction of long lasting immunity is critical for influenza vaccines, which might be used in pre-pandemic settings in order to provide sufficient protection at the time, when the pandemic hits the population. Therefore the data presented is highly relevant.

Major Compulsory Revisions

1. The title indicates that specific immune responses against H5N1 persist for 2 years. However, the data show that antibody levels decline substantially over the follow-up period. This should be better reflected in the title, the abstract and the discussion.

2. The usage of two influenza strains (homologous and heterologous to the vaccine strain) needs to be explained in the Material + Methods section.

3. The results for the two different influenza strains need to be discussed in more details. The heterologous strain is not mentioned at all in the introduction and in the discussion.

4. Statistical information needs to be added to all Figures. There is no indication of statistically significant differences between groups or time points.

Minor Essential Revisions

1. The follow-up study was done only with participants in Belgium. Is that in accordance with the original study protocol? If so, this should be stated in the Material + Methods section.

2. page 9, last paragraph: “… response against any of the two strains tested (Figure 2B-C)”. Figure 2 shows results for one of the strains. Please correct the text or the reference to the Figure.

3. The scales of the figures are quite arbitrary. I suggest harmonizing the scaling (e.g. Figure 3 B and C compared to Figure 2 B and C and Figure 5 A compared to Figure 6A)

Discretionary Revisions
1. In order to fully evaluate the residual antibody responses after 12-24 months a comparison with pre-vaccination data would be useful. I understand that these data have been previously published, but nevertheless it might be interesting to see whether/how far above baseline antibody titers are 12-24 months later. Maybe this information could at least be integrated in the text.

2. Cut-off levels of the assays should be shown in the Figures, e.g. as dashed lines (e.g. Figure 2 and 3 cut-off 10 for GMTs).

3. It would be interesting to see, whether antibody titers decline at slower after vaccination with adjuvanted vaccine. I suggest to calculate “half-life times” for antibody titers, if that is feasible.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.